FILE 'USPATFULL' ENTERED AT 10:12:18 ON 09 NOV 2004
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FILE 'MEDLINE' ENTERED AT 10:12:18 ON 09 NOV 2004

=> s biotin
L4 115239 BIOTIN

=> dup rem L4
115239 ANSWERS REQUESTED EXCEEDS MAXIMUM ALLOWED OF 50000
You may process up to 50,000 answers per command. Please try to
narrow your search until your resulting L# answer set is within the
maximum number of answers.

=> s homobiotin
L5 70 HOMOBIOTIN

=> s l4 and l5
L6 67 L4 AND L5

=> dup rem L6
PROCESSING COMPLETED FOR L6
L7 56 DUP REM L6 (11 DUPLICATES REMOVED)

=> d L7 kwic

L7 ANSWER 1 OF 56 CAPLUS COPYRIGHT 2004 ACS on STN
AB . . . of the agent. The three components are bound by a trifunctional linker. For example, rituximab (monoclonal antibody) was treated with 3-(13'-thioureabenzylDOTA)trioxadiamine-1-(13''-**biotin**-Asp-OH)trioxadiamine-5-isothiocyanato-aminoisophthalate and mixed with 111InCl3 and DTPA to obtain a conjugate.
ST lymphoma antibody nuclide **biotin** conjugate targeting immunoradiotherapy; rituximab **biotin** multifunctional linking conjugate radiolabeled lymphoma targeting
IT 58-85-5D, **Biotin**, immunoconjugates 60-00-4D, EDTA, radionuclide-labeled immunoconjugates 67-43-6D, DTPA, radionuclide-labeled immunoconjugates 533-48-2D, Desthiobiotin, immunoconjugates 669-72-7D, Norbiotin, immunoconjugates 1784-22-1D, **Homobiotin**, immunoconjugates 3376-83-8D, **Biotin** sulfoxide, immunoconjugates 7440-15-5D, Rhenium, immunoconjugates 7440-26-8D, Technetium, chelates, immunoconjugates 10043-66-0D, Iodine 131, immunoconjugates, biological studies 10098-91-6D, Yttrium 90, immunoconjugates, biological studies 13395-35-2D, Iminobiotin, immunoconjugates 13967-63-0D, Scandium 46, immunoconjugates, biological studies 13981-27-6D, Zirconium 89, immunoconjugates, biological studies 13981-56-1D, Fluorine 18, immunoconjugates, biological studies 13982-20-2D, Gold 193, immunoconjugates, biological studies 13982-22-4D, Gallium 72, immunoconjugates, biological studies 14158-30-6D, Iodine 124, immunoconjugates, biological studies 14158-31-7D, Iodine 125, immunoconjugates, biological studies 14265-75-9D, Lu 177, immunoconjugates, biological studies 14378-26-8D, Re 188, immunoconjugates, biological studies 14378-53-1D, Rhodium 101, immunoconjugates, biological studies 14391-96-9D, Scandium 47, immunoconjugates, biological studies 14474-91-0D, Oxybiotin, immunoconjugates 14809-47-3D, Bromine 75, immunoconjugates, biological studies 14913-49-6D, Bismuth 212, immunoconjugates, biological studies 14981-64-7D, Palladium 109, immunoconjugates, biological studies 14998-63-1D, Re 186, immunoconjugates, biological studies 15034-51-2D,

Gallium 73, immunoconjugates, biological studies 15092-94-1D, Lead 212, immunoconjugates, biological studies 15623-45-7D, Ra 223, immunoconjugates, biological studies 15690-69-4D, Palladium 100, immunoconjugates, biological studies 15715-08-9D, Iodine 123, immunoconjugates, biological studies 15750-15-9D, Indium 111, immunoconjugates, biological studies 15755-39-2D, At 211, immunoconjugates, biological studies 15757-14-9D, Gallium 68, immunoconjugates, biological studies 15757-86-5D, Copper 67, immunoconjugates, biological studies 15758-35-7D, Ruthenium 97, immunoconjugates, biological studies 15765-38-5D, Bromine 76, immunoconjugates, biological studies 15765-78-3D, Rhenium 189, immunoconjugates, biological studies 15766-00-4D, Samarium 153, immunoconjugates, biological studies 15776-20-2D, Bismuth 213, immunoconjugates, biological studies 17638-10-7D, Radium 212, immunoconjugates, biological studies 22342-46-7D, Diaminobiotin, immunoconjugates 29687-57-8D, Sm 157, immunoconjugates, biological studies 40720-05-6D, **Biotin** sulfone, immunoconjugates 56491-86-2D, NOTA, radionuclide-labeled immunoconjugates 60239-18-1D, DOTA, radionuclide-labeled immunoconjugates 60239-22-7D, TETA, radionuclide-labeled immunoconjugates 121806-83-5D, CITC-DTPA, radionuclide complexes, immunoconjugates 208921-02-2D, Tositumomab, radionuclide conjugates 378759-66-1D, Indium 114m, immunoconjugates, biological studies 378784-45-3D, Tc-99m, immunoconjugates, biological studies 713125-25-8D, antibody conjugates 714269-01-9D, antibody conjugates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-lymphoma targeting agents with effector and affinity functions linked by trifunctional reagent)

=> d L6 kwic IBIB

L6 ANSWER 1 OF 67 CAPLUS COPYRIGHT 2004 ACS on STN
AB . . . of the agent. The three components are bound by a trifunctional linker. For example, rituximab (monoclonal antibody) was treated with 3-(13'-thioureabenzylDOTA)trioxadiamine-1-(13''-**biotin**-Asp-OH)trioxadiamine-5-isothiocyanato-aminoisophthalate and mixed with 111InCl3 and DTPA to obtain a conjugate.
ST lymphoma antibody nuclide **biotin** conjugate targeting immunoradiotherapy; rituximab **biotin** multifunctional linking conjugate radiolabeled lymphoma targeting
IT 58-85-5D, **Biotin**, immunoconjugates 60-00-4D, EDTA, radionuclide-labeled immunoconjugates 67-43-6D, DTPA, radionuclide-labeled immunoconjugates 533-48-2D, Desthiobiotin, immunoconjugates 669-72-7D, Norbiotin, immunoconjugates 1784-22-1D, **Homobiotin**, immunoconjugates 3376-83-8D, **Biotin** sulfoxide, immunoconjugates 7440-15-5D, Rhenium, immunoconjugates 7440-26-8D, Technetium, chelates, immunoconjugates 10043-66-0D, Iodine 131, immunoconjugates, biological studies 10098-91-6D, Yttrium 90, immunoconjugates, biological studies 13395-35-2D, Iminobiotin, immunoconjugates 13967-63-0D, Scandium 46, immunoconjugates, biological studies 13981-27-6D, Zirconium 89, immunoconjugates, biological studies 13981-56-1D, Fluorine 18, immunoconjugates, biological studies 13982-20-2D, Gold 193, immunoconjugates, biological studies 13982-22-4D, Gallium 72, immunoconjugates, biological studies 14158-30-6D, Iodine 124, immunoconjugates, biological studies 14158-31-7D, Iodine 125, immunoconjugates, biological studies 14265-75-9D, Lu 177, immunoconjugates, biological studies 14378-26-8D, Re 188, immunoconjugates, biological studies 14378-53-1D, Rhodium 101, immunoconjugates, biological studies 14391-96-9D, Scandium 47, immunoconjugates, biological studies 14474-91-0D, Oxybiotin, immunoconjugates 14809-47-3D, Bromine 75, immunoconjugates, biological studies 14913-49-6D, Bismuth 212, immunoconjugates, biological studies 14981-64-7D, Palladium 109, immunoconjugates, biological studies

14998-63-1D, Re 186, immunoconjugates, biological studies 15034-51-2D, Gallium 73, immunoconjugates, biological studies 15092-94-1D, Lead 212, immunoconjugates, biological studies 15623-45-7D, Ra 223, immunoconjugates, biological studies 15690-69-4D, Palladium 100, immunoconjugates, biological studies 15715-08-9D, Iodine 123, immunoconjugates, biological studies 15750-15-9D, Indium 111, immunoconjugates, biological studies 15755-39-2D, At 211, immunoconjugates, biological studies 15757-14-9D, Gallium 68, immunoconjugates, biological studies 15757-86-5D, Copper 67, immunoconjugates, biological studies 15758-35-7D, Ruthenium 97, immunoconjugates, biological studies 15765-38-5D, Bromine 76, immunoconjugates, biological studies 15765-78-3D, Rhenium 189, immunoconjugates, biological studies 15766-00-4D, Samarium 153, immunoconjugates, biological studies 15776-20-2D, Bismuth 213, immunoconjugates, biological studies 17638-10-7D, Radium 212, immunoconjugates, biological studies 22342-46-7D, Diaminobiotin, immunoconjugates 29687-57-8D, Sm 157, immunoconjugates, biological studies 40720-05-6D, **Biotin** sulfone, immunoconjugates 56491-86-2D, NOTA, radionuclide-labeled immunoconjugates 60239-18-1D, DOTA, radionuclide-labeled immunoconjugates 60239-22-7D, TETA, radionuclide-labeled immunoconjugates 121806-83-5D, CITC-DTPA, radionuclide complexes, immunoconjugates 208921-02-2D, Tositumomab, radionuclide conjugates 378759-66-1D, Indium 114m, immunoconjugates, biological studies 378784-45-3D, Tc-99m, immunoconjugates, biological studies 713125-25-8D, antibody conjugates 714269-01-9D, antibody conjugates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-lymphoma targeting agents with effector and affinity functions linked by trifunctional reagent)

ACCESSION NUMBER: 2004:531387 CAPLUS
DOCUMENT NUMBER: 141:94296
TITLE: Anti-lymphoma targeting agents with effector and affinity functions linked by a trifunctional reagent
INVENTOR(S): Sandberg, Bengt; Nilsson, Rune
PATENT ASSIGNEE(S): Mitra Medical Technology Ab, Swed.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054615	A1	20040701	WO 2003-SE1949	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, EG, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2002-3731 A 20021213
US 2002-433012P P 20021213
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d L6 2-5 ABS IBIB

L6 ANSWER 2 OF 67 CAPLUS COPYRIGHT 2004 ACS on STN

AB We have studied the structural elements that affect ligand exchange between the two high affinity **biotin**-binding proteins, egg white avidin and its bacterial analog, streptavidin. For this purpose, we have developed a simple assay based on the antipodal behavior of the two proteins toward hydrolysis of biotinyl p-nitrophenyl ester (BNP). The assay provided the exptl. basis for these studies. It was found that **biotin** migrates unidirectionally from streptavidin to avidin. Conversely, the **biotin** derivative, BNP, is transferred in the opposite direction, from avidin to streptavidin. A previous crystallog. study provided insight into a plausible explanation for these results. These data revealed that the non-hydrolyzable BNP analog, biotinyl p-nitroanilide, was almost completely sheltered in streptavidin as opposed to avidin in which the disordered conformation of a critical loop resulted in the loss of several hydrogen bonds and concomitant exposure of the analog to the solvent. In order to determine the minimal modification of the **biotin** mol. required to cause the disordered loop conformation, the structures of avidin and streptavidin were determined with norbiotin, **homobiotin**, and a common long-chain **biotin** derivative, biotinyl ε-aminocaproic acid. Six new crystal structures of the avidin and streptavidin complexes with the latter **biotin** analogs and derivs. were thus elucidated. It was found that extending the **biotin** side chain by a single CH2 group (i.e. **homobiotin**) is sufficient to result in this remarkable conformational change in the loop of avidin. These results bear significant biotechnol. importance, suggesting that complexes containing biotinylated probes with streptavidin would be more stable than those with avidin. These findings should be heeded when developing new drugs based on lead compds. because it is difficult to predict the structural and conformational consequences on the resultant protein-ligand interactions.

ACCESSION NUMBER: 2002:658989 CAPLUS
DOCUMENT NUMBER: 138:35650
TITLE: Ligand exchange between proteins: exchange of **biotin** and **biotin** derivatives between avidin and streptavidin
AUTHOR(S): Pazy, Yael; Kulik, Tikva; Bayer, Edward A.; Wilchek, Meir; Livnah, Oded
CORPORATE SOURCE: Department of Biological Chemistry, The Institute of Life Sciences, The Wolfson Centre for Applied Structural Biology, The Hebrew University of Jerusalem, Jerusalem, 91904, Israel
SOURCE: Journal of Biological Chemistry (2002), 277(34), 30892-30900
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 67 CAPLUS COPYRIGHT 2004 ACS on STN

AB A method for the conditioning of an extracorporeal device is described, as well as a method for extracorporeal extraction of toxic material from mammalian body fluids in connection with diagnosis or treatment of a mammalian condition or disease. The methods comprise (i) a solution containing a reagent comprising **biotin** moieties, such as natural **biotin** or its derivs., and a toxin-binding moiety, (ii) linkers and a trifunctional crosslinking moiety, and (ii) an extracorporeal device comprising said reagent. For example, a dibiotin compound, 1-isothiocyanato-3,5-bis-(13'-biotinamidyl-4',7',10'-trioxatridecanamidyl)-aminoisophthalate was prepared and conjugated with a toxin-binding mol., i.e., monoclonal antibody 53-6A2. A dibiotin-toxin-binding conjugate was used for conditioning of an avidin-agarose column suitable for removal of toxins from blood.

ACCESSION NUMBER: 2001:923565 CAPLUS

DOCUMENT NUMBER: 136:42919
TITLE: **Biotin** derivatives for an extracorporeal device
INVENTOR(S): Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
PATENT ASSIGNEE(S): Mitra Medical Technology AB, Swed.; University of Washington
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095857	A2	20011220	WO 2001-SE1374	20010618
WO 2001095857	A3	20020328		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002159994	A1	20021031	US 2001-881213	20010615
AU 2001074761	A5	20011224	AU 2001-74761	20010618
EP 1289563	A2	20030312	EP 2001-941404	20010618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011726	A	20030527	BR 2001-11726	20010618
JP 2004503299	T2	20040205	JP 2002-510039	20010618
NO 2002005931	A	20030214	NO 2002-5931	20021211
US 2004052784	A1	20040318	US 2003-311150	20030423
PRIORITY APPLN. INFO.:			SE 2000-2287 A	20000616
			US 2000-216625P P	20000707
			WO 2001-SE1374 W	20010618

L6 ANSWER 4 OF 67 CAPLUS COPYRIGHT 2004 ACS on STN
AB An investigation was conducted in which the stabilities of four structurally different **biotin** derivs. were assessed with regard to biotinamide bond hydrolysis by the enzyme biotinidase. The **biotin** derivs. studied contained an extra methylene in the valeric acid chain of **biotin** (i.e., **homobiotin**), or contained conjugated amino acids having hydroxymethylene, carboxylate, or acetate functionalities on a methylene alpha to the biotinamide bond. The biotinidase hydrolysis assay was conducted on **biotin** derivs. that were radioiodinated at high specific activity, and then subjected to diluted human serum at 37° for 2 h. After incubation, assessment of biotinamide bond hydrolysis by biotinidase was readily achieved by measuring the percentage of radioactivity that did not bind with avidin. As controls, an unsubstituted **biotin** derivative which is rapidly cleaved by biotinidase and an N-methyl-substituted **biotin** derivative which is stable to biotinidase cleavage were included in the study. The results indicate that increasing the distance from the **biotin** ring structure to the biotinamide bond by one methylene only decreases the rate of biotinidase cleavage, but does not block it. The data obtained also indicate that placing a hydroxymethylene, carboxylate, or acetate alpha to the biotinamide bond is effective in blocking the biotinamide hydrolysis reaction. These data, in combination with data previously obtained, which indicate that **biotin** derivs. containing hydroxymethylene or carboxylate moieties retain the slow dissociation rate of **biotin** from avidin and streptavidin [Wilbur, D. S., et al. (2000)

Bioconjugate Chemical 11, 569-583], strongly support incorporation of these structural features into **biotin** derivs. being used for in vivo targeting applications.

ACCESSION NUMBER: 2001:408721 CAPLUS
DOCUMENT NUMBER: 135:134197
TITLE: **Biotin** reagents for antibody pretargeting. 5. Additional studies of **biotin** conjugate design to provide biotinidase stability
AUTHOR(S): Wilbur, D. Scott; Hamlin, Donald K.; Chyan, Ming-Kuan; Kegley, Brian B.; Pathare, Pradip M.
CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chemistry (2001), 12(4), 616-623
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 67 CAPLUS COPYRIGHT 2004 ACS on STN
AB An investigation was conducted to determine the affect of structural variation of **biotin** conjugates on their dissociation rates from Av and SAv. This information was sought to help identify optimal **biotin** derivs. for in vivo applications. Fifteen **biotin** derivs. were conjugated with a cyanocobalamin (CN-Cbl) derivative for evaluation of their "relative" dissociation rates by size exclusion HPLC anal. Two **biotin** -CN-Cbl conjugates, one containing unaltered **biotin** and the other containing iminobiotin, were prepared as reference compds. for comparison purposes.

The first structural variations studied involved modification of the biotinamide bond with a N-Me moiety (i.e., sarcosine conjugate), lengthening the valeric acid side chain by a methylene unit (i.e., **homobiotin**), and replacing the biotinamide bond with thiourea bonds in two conjugates. The rate of dissociation of the **biotin** -CN-Cbl derivative from Av and SAv was significantly increased for **biotin** derivs. containing those structural features. Nine addnl. **biotin** conjugates were obtained by coupling amino acids or functional group protected amino acids to the **biotin** moiety. In the conjugates, the **biotin** moiety and biotinamide bond were not altered, but substituents of various sizes were introduced α to the biotinamide bond. The results obtained from HPLC analyses indicated that the rate of dissociation from Av or SAv was not affected by small substituents α to the biotinamide (e.g., Me, hydroxymethyl, and carboxylate groups), but was significantly increased when larger functional groups were present. On the basis of the results obtained, it appears that **biotin** conjugates which retain an unmodified **biotin** moiety and have a linker mol. conjugated to it that has a small functional group (e.g., hydroxymethylene or carboxylate) α to the biotinamide bond are excellent candidates for in vivo applications. These structural features are obtained in the **biotin** amino acid conjugates: **biotin**-serine, **biotin**-aspartate, **biotin** -lysine, and **biotin**-cysteine. Importantly, these **biotin** derivs. can be readily conjugated with other mols. for specific in vivo applications. In our studies, these derivs. will be used in the design of new **biotin** conjugates to carry radionuclides for cancer therapy using the pretargeting approach.

ACCESSION NUMBER: 2000:433866 CAPLUS
DOCUMENT NUMBER: 133:248664
TITLE: **Biotin** Reagents for Antibody Pretargeting. 4. Selection of **Biotin** Conjugates for in Vivo Application Based on Their Dissociation Rate from Avidin and Streptavidin
AUTHOR(S): Wilbur, D. Scott; Chyan, Ming-Kuan; Pathare, Pradip M.; Hamlin, Donald K.; Frownfelter, Milah B.; Kegley,

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DICTIONARY FILE UPDATES: 7 NOV 2004 HIGHEST RN 776240-21-2

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=> s biotin
L1 1430 BIOTIN

=> s ?biotin?
LEFT TRUNCATION IGNORED FOR '?BIOTIN?' FOR FILE 'REGISTRY'
L2 1430 BIOTIN?
Left truncation is not valid in the specified search field in the
specified file. The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

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used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> s homobiotin
L3 20 HOMOBIOTIN

=> file caplus uspatfull biosis embase medline

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FULL ESTIMATED COST	16.65	16.92

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